

May 9, 2002

David Brandwene  
Akzo Nobel Chemicals Inc.  
5 Livingstone Avenue  
Dobbs Ferry, New York 10522

Dear Mr. Brandwene:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Trixylenyl Phosphate, posted on the ChemRTK HPV Challenge Program Web site on October 10, 2001. I commend Akzo Nobel Chemicals Inc. for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its HPV Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

While we appreciate your efforts to summarize the adequacy of the available data in a matrix (the Test Plan), it would be informative if a discussion was provided describing how you arrived at the conclusions regarding the adequacy of data available for the various endpoints. In addition, the OECD test guideline should be stated for any proposed testing. As noted in our comments, OECD TG 422 is recommended to address the repeat dose and reproductive/developmental toxicity endpoints. Also, genetic toxicity testing should be performed using in vitro protocols unless a specific justification is presented.

EPA will post this letter and the attached Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Akzo Nobel Chemicals Inc. advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at [tsca-hotline@epa.gov](mailto:tsca-hotline@epa.gov).

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director  
Risk Assessment Division

Attachment

cc: W. Sanders  
A. Abramson  
C. Auer  
M. E. Weber

## **EPA Comments on Chemical RTK HPV Challenge Submission: Trixylenyl Phosphate**

### **SUMMARY OF EPA COMMENTS**

The sponsor, Akzo Nobel Chemicals Inc., submitted a test plan and robust summaries to EPA for Trixylenyl phosphate (CAS# 25155-23-1) dated September 7, 2001. EPA posted the submission on the ChemRTK HPV Challenge Web site on October 10, 2001.

EPA has reviewed this submission and has reached the following conclusions:

1. Test Substance Identification. Because the name and CAS No. do not adequately define this substance, the submitter needs to supply some discussion of the substance identity for the submitted robust summaries as well as all test material to be used to develop data proposed in the test plan. In addition, EPA considers the characterization of the substance in some submitted robust summaries insufficient to determine the adequacy of some endpoints.
2. Physicochemical Data. EPA agrees with the submitter that testing is needed for water solubility.
3. Environmental Fate and Pathways. EPA agrees with the submitter's proposed testing for photodegradation, stability in water, and fugacity. The robust summary for biodegradation provided by the submitter is inadequate and thus testing is needed for this endpoint.
4. Health Effects Toxicity. (a) No further testing is required for acute toxicity. (b) The results for *in vitro* testing for gene mutations are adequate, provided the substance was tested up to the limits of its solubility (see Specific Comments on Robust Summaries). (c) EPA agrees with the submitter's proposal to do chromosomal aberrations testing, repeated-dose testing, reproductive and developmental toxicity testing. The chromosomal aberrations testing should be done using an *in vitro* protocol and the later three endpoints should be addressed using the combined protocol (OECD TG 422).
5. Ecotoxicity. The results for acute toxicity testing in fish are not adequate because it was probably tested above the water solubility limit and the test concentrations were not measured. The stability and solubility of the test substance have not been adequately characterized. The submitter needs to conduct testing using a flow-through system with measured concentrations. A chronic daphnid test may be necessary to address this endpoint.

EPA is requesting that the submitter advise the Agency within 60 days of any modifications to its submission.

### **EPA COMMENTS ON THE TRIXYLENYL PHOSPHATE CHALLENGE SUBMISSION**

#### **Test Plan**

Chemistry (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

EPA agrees with the submitter that testing is needed to define the water solubility for this chemical.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

EPA agrees that testing is needed for photodegradation, stability in water and fugacity.

*Biodegradation*. Details are lacking in the robust summary concerning the submitter's approach to assessing biodegradation. There is not enough information for EPA to determine the adequacy of the study (see Specific Comments on Robust Summaries below). EPA believes testing is needed to satisfy

this endpoint.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

The submitter provided adequate information on acute toxicity. EPA agrees with the submitter that testing is needed for repeated-dose, reproductive and developmental toxicity. To address these endpoints under the HPV Challenge Program, EPA recommends the use of the combined protocol (OECD TG 422, see 65 FR 81695). EPA agrees that existing data are adequate for gene mutations, provided the substance was tested up to the limits of its solubility (see Specific Comments on the Robust Summaries). For chromosomal aberrations, testing is needed to address this endpoint (the submitter has proposed genetic testing without specifying the endpoint or test guideline). For this endpoint EPA recommends an in vitro protocol (see 65 FR 81695).

Ecological Effects (fish, daphnia, and algal toxicity)

EPA agrees with the submitter that testing is necessary in order to assess acute toxicity to aquatic invertebrates and aquatic plants.

*Acute Toxicity to Fish.* EPA considers the test inadequate because the chemical appears to have been tested above its water solubility and without measured concentrations. Information on the chemical's stability and solubility in water will be important in designing an adequate study and determining if additional tests are needed, such as a daphnid chronic test. For chemicals with Log P values of  $\geq 4.2$  chronic testing may be needed. For more information and guidance pertaining to difficult-to-test substances and chemicals with high log P values refer to the OECD Web site at <http://www.oecd.org/ehs/test/monos.htm>.

**Specific Comments on the Robust Summaries**

Generic comments.

The following comments apply to all the robust summaries provided by the submitter. In general, the robust summaries did not provide enough detail. The submitter should consult EPA guidance documents for the preparation of robust summaries (<http://www.epa.gov/chemrtk/guidocs.htm>).

Each summary should clearly identify the test substance by the chemical name and include information on the percent composition of constituents. In the robust summaries, the submitter often referred to a section of the IUCLID document with a generic description of the chemical. The identity of the actual test substance and its purity was not specifically stated in each robust summary. In addition, some summaries referred to trade name products which were insufficiently described.

Environmental Fate and Pathways

*Biodegradation.* The robust summary is inadequate for assessing the study and determining if it satisfies the purposes of the HPV Challenge Program. It fails to provide information on the method used (OECD guideline number), test conditions, compliance with GLPs, and test substance. The submitter also needs to provide more detailed information on degradation, kinetics of test substance, and results. EPA is unable to assess this endpoint without additional data.

Health Effects

*Genetic toxicity.* The robust summaries provided for the Ames test lacked important details, such as the rationale for dose selection, information on the use of a positive reference substance and negative

controls, and details of response including values showing that the test results were negative. In addition, the substance needs to be tested up to the limits of its water solubility. Since several values for water solubility appear in the robust summaries, there are unresolved questions about the appropriate value.

#### Ecotoxicity

*Acute Toxicity to Fish.* EPA considers the test inadequate because nominal concentrations were used and measured values are needed.

#### **Followup Activity**

EPA is requesting that the submitter advise the Agency within 60 days of any modifications to its submission.